

Scientific Abstract

This study will evaluate the safety of allogeneic donor lymphocyte infusions in patients with relapsed hematologic malignancies after allogeneic bone marrow transplantation (BMT). Donor lymphocyte infusions have resulted in the cure of some patients with relapsed leukemia or lymphoproliferative disorders after allogeneic BMT, but have been complicated by the development of graft versus host disease (GvHD).

A VSV-G pseudotyped Moloney murine leukemia retroviral vector transferring a novel chimeric suicide gene was developed. The suicide gene is composed of the extracellular and transmembrane domains of the human CD34 cDNA, fused in frame to a genetically modified and highly active variant of the Herpes Simplex thymidine kinase (CD34-TK75). This highly active variant of the Herpes Simplex thymidine kinase allows efficient killing of transduced, gene expressing T cells by the drug ganciclovir (GCV). The pseudotyped vector in conjunction with T cell stimulation in the presence of CD3/CD28 antibody coated beads provides for improved transduction efficiency into the target cell population. Transduced, CD34-TK75 expressing T cells can easily be enriched to over 95% purity using a clinical CD34+ cell separator.

Infused into patients with relapsed hematologic malignancies after allogeneic BMT, these transduced, selected allogeneic T cells may elicit an anti-leukemia response while allowing for the adverse effects of GvHD (if it develops) to be mitigated by the administration of GCV, and for T cells involved in GvHD to be eliminated.